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Optical activity retention in the reaction of magnesium with (+)-R-1-chloro-1-phenylethane

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Abstract

Optical activity retention has been proved in the course of the formation of Grignard reagent from optically active (+)-R-1-chloro-1-phenylethane.

Key words: Magnesium; Optical activity

1. Introduction

In many recent studies, optically active compounds have been used as starting materials in organic synthesis for investigation of reaction mechanisms. Optical activity retention and the presence of an asymmetric centre in the benzyl halide molecule must be the most reliable evidence of an ion-radical mechanism for the Grignard reaction.

It is well known that there is no optical activity retention in reactions of magnesium with alkyl- and aryl halides. The only result of these reactions is racemization [1,2]. The configuration of the asymmetric centre can be partially retained in the reactions of unsaturated and very strained cycloalkyl halides and almost completely retained in reactions of the most stable radicals with high inversion barrier [3–6].

The main cause of racemization in Grignard reactions is stereochemical instability of C–Mg bond and this can arise just after Grignard reagent formation [7]. The configuration of the Grignard reagent must be fixed at the moment of its formation. It can be achieved by carrying out this reaction in the presence of deuterium labelled alcohols which react very rapidly with Grignard reagents with optical activity retention [5,6].

We have investigated the reaction of optically active (+)-R-1-chloro-1-phenylethane (**1**) with magnesium to seek experimental evidence of optical activity retention at the asymmetry centre in the course of formation of benzylmagnesiumhalides. This reaction was carried out both with and without t-BuOD (Scheme 1).

The result of this reaction was the formation of optically active 1-phenylethane-1D (**2**) with a yield of 88% and optical purity 6.2% and three other unlabelled hydrocarbons **3**, **4** and **5** (total yield 10%). The formation of optically active **2** might be clear evidence for partial formation of Grignard reagent on the magnesium surface via an intermediate ion-radical without any charge separation. Nevertheless the contribution of radical mechanism can be important as well. Partially deuterium labelled racemic 1-phenylethane-1D (**6**) with a total proportion of deuterium in the CH_2 group of 93.5% was obtained in the absence of t-BuOD after treatment of the reaction mixture with D_2O.

Comparison of the optical purity of **2** (6.2%) and of the proportion of deuterium in 1-phenylethane-1D both lead us to conclude that racemization of benzylmagnesiumhalide takes place, through fast structure inversion, just after its formation.

The large amount of deuterium in the reaction products is clear evidence that this reaction proceeds on the magnesium surface within a solvent cage. If it were not so, we would expect only a small amount of deuterium in **2** because of the disproportionation of the 1-phenylethyl radical and its reaction with solvent [8]. The formation of a racemic mixture of **3** and **4**

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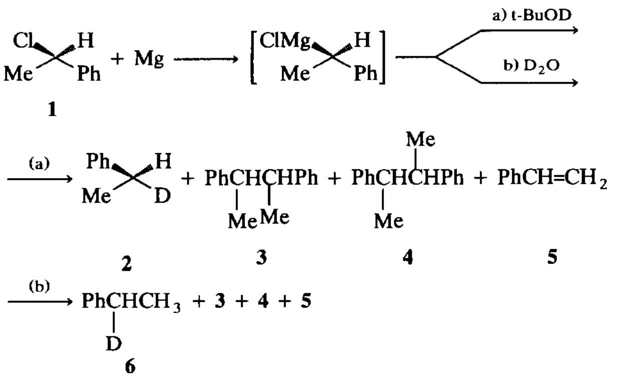

Scheme 1.

while **1** is reacting with Mg, in cases (a) and (b), shows that recombination of 1-phenylethyl radicals can proceed after they enter solution.

2. Experimental details

2.1. Syntheses

Synthesis of (+)-R-1-chloro-1-phenylethane (**1**) was carried out by interaction of (−)-S-1-phenylethanol with PCl_{3D} in the presence of pyridine in pentane solution. Yield 74%, b.p. 80–81°/17 mm. $[\alpha]^{25}_{D} = +94.1°$ ($c = 1$). ^{1}NMR ($CDCl_3$, int. TMS, 90 MHz): δ(ppm) = 1.68 (d, 3H, CH_3); 4.86 (q, 1H, CH); 7.14 (m, 5H, arom). Lit. data: b.p. 78–82°/17 mm, $[\alpha]^{25}_{D} = +125.4°$ ($c = 1$) [9].

Synthesis of (−)-S-1-phenylethanol was carried out in accordance with [10]. Yield 55%, b.p. 94–95°/14 mm, $[\alpha]^{25}_{D} = -37.65°$ ($c = 1$). ^{1}NMR ($CDCl_3$, int. TMS, 90 MHz): δ(ppm) = 1.21 (d, 3H, CH_3); 3.78(q, 1H, CH); 7.06 (m, 5H, arom). Lit. data: b.p. 94.5–95°/14 mm, $[\alpha]^{25}_{D} = -44.2°$ ($c = 1$) [10].

Synthesis of t-BuOD was carried out in accordance with [11]. Yield 70%, b.p. 80–82°, m.p. 25–25.5°. ^{1}NMR ($CDCl_3$, int. TMS, 90 MHz): δ(ppm) = 1.25 (s, 9H, $3CH_3$). Lit. data: b.p. 80–82°, m.p. 24–25° [11].

2.2. Reactions

Reaction of **1** with magnesium in the presence of t-BuOD. To a suspension of magnesium powder (200 mmol) in dry ether at 0° was added 200 mmol of t-BuOD and finally a solution of 50 mmol (+)-R-1-chloro-1-phenylethane in dry ether for 20 min. The reaction mixture was stirred for 1 h at 0°. After filtration the ether was removed and the residue was chromatographed on silica gel.

Reaction of **1** with magnesium without presence of t-BuOD. To a suspension of magnesium powder (200 mmol) in dry ether at 0° was added a solution of 50 mmol (+)-R-1-chloro-1-phenylethane in dry ether within 20 min. The reaction mixture was stirred for 1 h at 0° and finally was quenched with 75 mmol D_2O. After separation the ether solution was filtered and dried. The solvent was removed and the residue chromatographed on silica gel.

(+)-S-1-Phenylethane-1D (**2**). Yield 88%, b.p. 135–136°, n^{20}_{D} 1.4954, $[\alpha]^{20}_{D} = +0.05°$ ($c = 1$). ^{1}NMR ($CDCl_3$, int. TMS, 90 MHz): δ(ppm) = 1.23 (d, 3H, CH_3); 2.62 (q, 1H, CH); 7.20 (m, 5H, arom). Lit. data: b.p. 135–136°, $n^{20}_{D} = 1.4919$ [12], $[\alpha]^{20}_{D} = +0.81°$ [13].

Mixture of RS-1-phenylethane-1D and RS-1-phenylethane, 93.5 : 6.5(**6**). Yield 80%. ^{1}NMR ($CDCl_3$, int. TMS, 90 MHz): δ(ppm) = 1.20 (d, 3H, CH_3), 93.5%; 1.24 (t, 3H, CH_3), 6.5%; 2.62 (q, 1H, CH), 93.5%; 2.66 (m, 2H, CH_2), 6.5%; 7.19 (m, 5H, arom).

RR,SS-2,3-Diphenylbutane (**3**). Yield 5% (quenched with t-BuOD), 8% (quenched with D_2O), b.p. 130–132°/7 mm, $n^{20}_{D} = 1.5557$. ^{1}NMR($CDCl_3$, int. TMS, 90 MHz): δ(ppm) = 1.17 (d, 6H, $2CH_3$); 2.76 (m, 2H, CH–CH); 7.24 (m, 10H, arom). Lit. data: b.p. 130–132°/7 mm [14], $n^{20}_{D} = 1.5555$ [15].

RS,RS-2,3-Diphenylbutane (**4**). Yield 5% (quenched with t-BuOD) 7% (quenched with D_2O), b.p. 144–149°/12 mm, m.p. 126–127°. ^{1}NMR($CDCl_3$, int. TMS, 90 MHz): δ(ppm) = 1.03 (d, 6H, $2CH_3$); 2.75 (m, 2H, CH–CH); 7.24 (m, 10H, arom). Lit. data: b.p. 143–150°/12 mm [14], m.p. 126–127° [15].

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